

## **REMARKS**

Claims 31-71 are currently pending in the subject application and have been examined on the merits.

Claims 31-71 have been finally rejected under 35 U.S.C. § 112, ¶ 1, as purportedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains to make and/or use the invention. In other words, claims 31-71 have been rejected as purportedly failing to comply with the enablement requirement.

Applicants respectfully traverse this rejection. Applicants have previously addressed this outstanding enablement rejection with arguments and evidence submitted with Applicants' *Response to Office Action* filed December 16, 2005 together with the *Declaration of Katherine C. Faria* ("*Faria Declaration*") and with the *37 C.F.R. § 1.114 Response to Office Action* filed December 6, 2006 together with the *Second Declaration of Katherine C. Faria* ("*Second Faria Declaration*").

In response to Applicants' arguments and evidence, the Examiner issued a *Final Office Action* on March 15, 2007 ("*Final Office Action*") in which it is stated that Applicants' arguments were not fully persuasive in that the scope of the term "culturing conditions" is not limited to the disclosure of culture media alone but encompasses conditions under which a designated media is used to make the cultured skin construct as claimed. *Final Office Action*, page 6. Specifically, the Final Office Action stated that like "in vivo" conditions, hormones and growth factors are known to play a role for cell growth and extracellular matrix synthesis in "in vitro" cell culture system. Further, the Final Office Action stated that the state of the art teaches that the identification of the "culture conditions" along with the "contents of chemically defined culture media" are the most important aspects required for the development of an artificial skin construct of clinical relevance, which would enable one skilled in the art to practice the invention as claimed without further undue amount of experimentation. As such, the Final Office Action stated that since the instant claims fail to recite the culturing conditions, the claims do not adequately define the instant invention. *Final Office Action*, pages 8-10.

Applicants respectfully disagree and submit that the *Faria Declaration* and the *Second Faria Declaration* fully addressed the outstanding enablement rejection. Nevertheless, in the interest of completing the evidentiary record before proceeding to appeal, Applicants thus file

this 37 C.F.R. § 1.116 Response To Office Action and the *Third Declaration Of Katherine C. Faria* (“*Third Faria Declaration*”) to address the Examiner’s State of the Art and Predictability argument in this *Final Office Action*.

Applicants have previously provided an analysis of the eight *Wands* factors in their previous responses which are herein incorporated by reference. Applicants thus further submit the following analysis for *Wands* factors (6 and 8) with respect to the specific “culturing conditions” argument advanced by the Examiner in this *Final Office Action*:

6. The Amount Of Direction Provided

The present Specification provides ample directions on how the culturing conditions necessary to prepare the tissue construct of the invention. For example, the Specification discloses that the matrix-producing cell can be grown on any biologically compatible material to which the cells can adhere and provide anchoring means for the cell-matrix construct to form. Specifically, the Specification discloses that the cultured tissue constructs of the invention do not rely on synthetic or bioresorbable members for the formation of the tissue construct (e.g., Specification, p. 9, line 1 to p.10 line 22). *Third Faria Declaration*, ¶ X.

Further, the Specification also specifically discloses how to supplement the basic media with amino acids, growth factors and hormones like insulin, transferrin, triiodothyronine, hydrocortisone etc. to grow and expand fibroblast cells (e.g., Specification page 12, line 30, to page 16 line 2). *Third Faria Declaration*, ¶ X.

The Specification also discloses how to supplement the basic media with ascorbate, proline, glycine and a neutral polymer to prepare a layer of extracellular matrix from dermal fibroblast cells in the absence of exogenous matrix components (e.g., Specification, page 16, line 3 to page 17, line 9). *Third Faria Declaration*, ¶ X.

Overall, the Specification meticulously discloses all of the culturing conditions necessary to prepare the tissue culture of the invention (e.g., page 11, line 25 to page 17, line 24). *Third Faria Declaration*, ¶ X.

Accordingly, the Specification provides ample guidance for practicing the claimed invention. *Third Faria Declaration*, ¶ X.

8. The Quantity Of Experimentation Needed

The quantity of experimentation needed, if any, would not be undue. The Specification discloses the optimization of culturing conditions for inducing human fibroblasts to produce a layer of extracellular matrix in the absence of both exogenous matrix components and a mesh member and for growing epidermal cells to form the cultured skin constructs of the present invention. (Factor 6, *supra*). *Third Faria Declaration*, ¶ X.

As such, for the reason set forth above, Applicants respectfully submit that the Specification is enabling for the pending claims and request that the rejection of claims 31-71 under 35 U.S.C. § 112, ¶ 1 be reconsidered and withdrawn.

The Examiner's Wand Factor Analysis and Arguments Are Incorrect

Applicants respectfully submit that analysis/arguments by the Examiner are incorrect and merit the withdrawal of this rejection.

For example, the Examiner argues that without the recitation of all the critical limitation (e.g., the culturing conditions), the claims do not adequately define the instant invention. (e.g., *Office Action*, page 7).

However, as set forth in the previous responses, the test for enablement is “whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with the information known in the art without undue experimentation” (emphasis added). *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988); *United States v. Telecommunications, Inc.*, 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988). Accordingly, as set forth above, Applicants submit that the formulations of the defined culture media and of the culturing conditions are extensively disclosed in the Specification, are well known in the art and do not need to be recited in the claims (e.g., *Faria Declaration*, ¶¶ 9, 11 and 13, *Second Faria Declaration*, ¶ 15, page 11, line 25 to page 17, line 24, *Final Office Action* pages 8-10). *Third Faria Declaration*, ¶ X.

Further, the Examiner argues that in the instant case it is unclear how one would envision the invention as claimed to avoid infringement issues especially when the process of making a cultured skin construct is multi-factorial and when the state of the art clearly teaches the role of

various growth factors for the development of an artificial skin construct. (e.g., *Office Action*, page 7). As set forth above, Applicants submit that the right question is whether the Specification teaches one of ordinary skill in the art how to practice each “event” without undue experimentation and not how one would envision the inventions as claimed to avoid infringement. *Third Faria Declaration*, ¶ X.

Additionally, Applicants submit that the “specialized cultured conditions” disclosed in “State of the Art” section at pages 8-10 of the Office Action are fully disclosed in the present Specification which provides ample guidance to one skilled in the art for practicing the claimed invention (e.g., Specification page 11, line 25 to page 17 lines 24). *Third Faria Declaration*, ¶ X.

As such, for all the reasons set forth above, Applicants respectfully submit that the Specification is enabling for the pending claims and request that the rejections of claims 31-71 under 35 U.S.C. § 112, ¶ 1 be reconsidered and withdrawn.

**CONCLUSION**

The application is now believed to be in proper condition for allowance and a Notice to that effect is respectfully requested. The Examiner may address any questions raised by this submission to the undersigned at (617) 832-1000. If any fees are due, the Commissioner is hereby authorized to credit any overpayment or charge any deficiencies to Deposit Account No. **Deposit Account No. 06-1448, Reference No. OGA-010.02.**

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